AJNR

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AJNR Am J Neuroradiol 2007, 28 (7) 1369-1370
doi: https://doi.org/10.3174/ajnr.A0545
http://www.ajnr.org/content/28/7/1369

CASE REPORT

Combined Pituitary Hormone Deficiency and PROP-1 Mutation in Two Siblings: A Distinct MR Imaging Pattern of Pituitary Enlargement

L.L.F. do Amaral
R.M. Ferreira
N.P.F.D. Ferreira
R.A. Mendonça
V.H.R. Marussi
J.L. da Cunha
B.R. Maçaranduba
J.D. Medeiros

SUMMARY: Mutations of the PROP-1 gene are the most frequent genetic defect in patients with combined pituitary hormone insufficiency. We present the cases of 2 siblings with PROP-1 mutations whom we observed longitudinally. Their initial pituitary MR imaging examinations showed identical findings: an enlarged adenohypophysis, with striking hypointensity on T2-weighted images and slight hyperintensity on T1-weighted images. In one of the children, the follow-up MR imaging obtained 3 years after hormonal replacement revealed a decrease in the size of the anterior pituitary lobe.

Disturbances of single transcriptional factors can lead to combined pituitary hormone deficiency (CPHD). The Prophet of Pit-1 (PROP-1) protein is one of these transcription factors.[1,2] The PROP-1 gene plays an essential role in the evolution of pituitary cells secreting growth hormone (GH), prolactin, thyroid-stimulating hormone (TSH), leuteinizing hormone, and follicle-stimulating hormone.[1,3,4] It accounts for approximately 50% of genetically determined CPHD.[5,6] We report the cases of 2 siblings with PROP-1 defects whom we observed longitudinally.

Case Reports

Two consanguineous siblings were referred for evaluation of growth failure in 2003. Patient #1, the older brother, was a 10-year-old boy. He was born at term after an uneventful pregnancy by spontaneous delivery. Birth length was normal. Patient #2 was a 7-year-old girl. She also was born by normal delivery, at term, with a normal birth length. Failure to thrive was noticed in both children when they were 4 years old. Their neuropsychomotor development was considered normal. The diagnosis of CPHD for GH, prolactin, and TSH was made by clinical data and standard stimulation tests in both patients. Exon 2 of the PROP-1 gene was amplified by polymerase chain reaction (PCR) from the children's genomic DNA, and a 2-bp deletion allele was confirmed.

The 2 siblings underwent the first pituitary MR imaging examination (Figs 1 and 2) in 2003. In patient #1, examination revealed a slightly enlarged adenohypophysis with 10-mm height, high signal intensity on T1-weighted images, and a striking hypointensity on T2-weighted images, without significant enhancement after contrast infusion. The stalk and the neurohypophysis were normal. In patient #2, examination showed exactly the same findings.

They were treated with complete hormonal replacement, with good improvement of growth velocity.

We performed additional follow-up MR imaging 3 years later. In the younger child, the gland showed a decrease in size (6 mm), but it remained with the same signal intensity on T1-weighted and T2-weighted images that had been observed in the previous examination. In the older brother, the new examination did not show significant changes compared with the first examination. We performed all MR imaging examinations with 1.5T scanners.

Discussion

In contrast to patients with CPHD of other genetic origins who show symptoms soon after birth, neonates with PROP-1 defects lack perinatal signs of hypopituitarism and generally have normal birth lengths.[1,3,6] Most patients present initially with profound growth retardation at a mean age of 4 years.[6]

Previous data regarding the pituitary size in humans with PROP-1 mutation was not consistent. Most MR imaging reports of PROP-1 mutations show a hypoplastic anterior pituitary lobe.[3,4,7,8] Fofanova et al[7] reported hypoplasia in 7 patients.

Voutetakis et al[3] described some patients with gland enlargement on MR imaging. Mendonça et al[9] and Riepe et al[1] reported enlarged adenohypophysis with high signal intensity on T1-weighted images and a marked reduction in height in the follow-up of patients with PROP-1 mutation. Nevertheless, none of these studies have reported the MR imaging pituitary findings on T2-weighted images.

We assume that the gland enlargement observed in our patients is related to an increased size of the adenohypophysis, with an important hypointensity on T2-weighted images. There was no mass but an abnormality involving the entire anterior pituitary lobe. The adenohypophysis may vary in size and shrink after hormonal replacement, but it remains with the same pattern of signal intensity on MR imaging. Consequently, T2-weighted images are very useful in such cases.

Unfortunately, we are not able to characterize the substance responsible for these abnormal and striking features on T2-weighed images because none of our patients were submitted to any kind of surgical procedure, and clinical management is the rule in such cases. A high protein content might be considered.

Regarding the pituitary stalk and posterior lobe, MR images showed a clearly normal aspect, just as the other cases

Received September 23, 2006; accepted November 27.

From the Department of Neuroradiology (L.L.F.d.A., R.M.F., N.P.F.D.F., R.A.M., V.H.R.M.), Medimagem, Hospital Beneficência Portuguesa, São Paulo, Brazil; and the Department of Endocrinology (B.R.M., J.L.d.C., J.D.M.), Hospital Brigadeiro, São Paulo, Brazil.

Address correspondence to Rafael Ferreira, Neuroradiology, Medimagem, Rua Martiniano de Carvalho, 960, AP 101, Bela Vista, São Paulo, São Paulo, 01321000, Brazil; e-mail: imagemrafael@hotmail.com

DOI 10.3174/ajnr.A0545

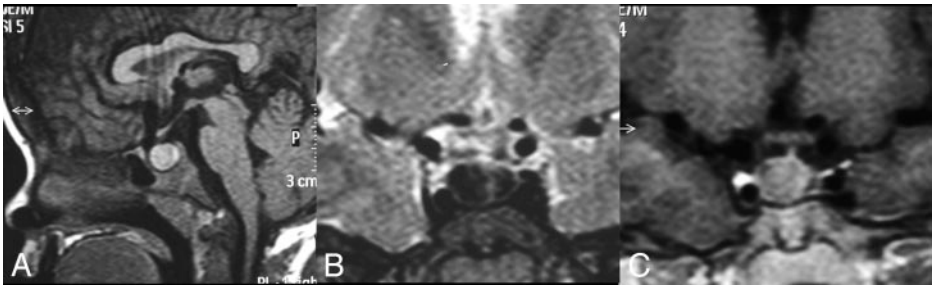

Fig 1. Patient #1 (the older brother): MR examination performed in 2003 shows an enlarged adenohypophysis with slightly high signal intensity on T1-weighted images (*A*), striking hypointensity on T2-weighted image (*B*), and no significant enhancement after contrast infusion (*C*).

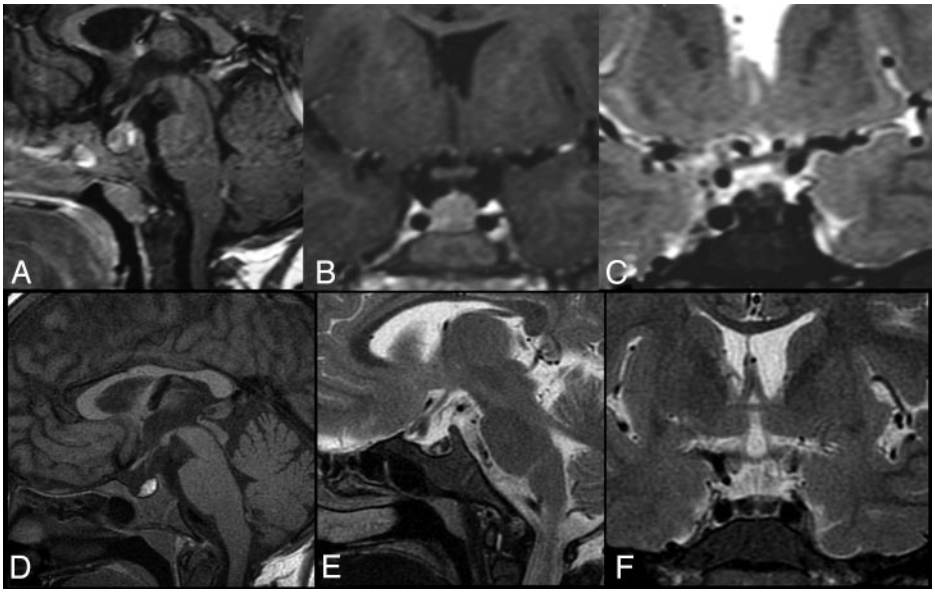

Fig 2. Patient #2 (the younger child): Her first MR examination reveals exactly the same imaging findings observed in the older brother (*A–C*). Examination performed 3 years later shows a slight regression in the size of the adenohypophysis, but it remains with the same striking hypointensity on T2-weighted image (*D–F*).

described in the literature, once the PROP-1 gene is expressed only in the anterior pituitary lobe.[1,3,7]

In summary, we advocate that in the clinical setting of a child with CPHD associated with an enlarged adenohypophysis (or small-sized after hormonal replacement) who presents with slight hyperintensity on T1-weighted images and a striking hypointensity on T2-weighted images, the PROP-1 gene mutation should be suspected and genetic analyses be performed.

As far as we know, such a distinct MR imaging pattern of adenohypophysis enlargement with striking hypointensity on T2-weighted images attributable to PROP-1 mutation has never been described in the radiologic literature.

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